AMENDMENTS TO THE SPECIFICATION

Please amend the specification as shown:

Please delete the paragraphs on page 4, lines 10-32 and replace them with the following paragraphs:

In another aspect of the present invention, there is provided a bidentate motif capable of binding to a cytoplasmic protein comprising a tyrosine and a serine/threonine residue, said motif consisting of the following sequence alignment:

N-X-X-Y- (X) $_{1-13}$-[R/K/H/Q]-[X/Ψ] $_{2-3}$-S/T-X-P **(SEQ ID NO: 71)**

wherein X is any residue, Y is tyrosine, S/T is serine or threonine and Ψ is a ~~hydrophibic~~hydrophobic residue or an equivalent thereof.

In yet another aspect of the present invention, there is provided a bidentate motif of a receptor capable of binding to a cytoplasmic protein comprising a tyrosine and a serine/threonine residue, said motif consisting of the following sequence alignment:

Y- (X) $_{1-16}$-[R/K/H/Q]-[X/Ψ] $_{2-3}$-S/T-X-P **(SEQ ID NO: 72)**

wherein X is any residue, Y is tyrosine, S/T is serine or threonine and Ψ is a ~~hydrophibic~~hydrophobic residue or an equivalent thereof.

In yet another aspect of the present invention, there is provided a bidentate motif capable of binding to a cytoplasmic protein comprising a tyrosine and a serine/threonine residue, said motif consisting of the following sequence alignment:

N-X-X-Y-[X]$_{1-30}$-[R/K/Q/H]-[X]$_{1-4}$-[S/T]-X-p **(SEQ ID NO: 73)**

wherein X is any residue, Y is phosphotyrosine, S/T is phosphoserine/phosphothreonine.

Please delete the paragraph on page 8, line 29 and replace it with the following paragraph:

Figure 9 shows the amino acid sequence of the common βc **(SEQ ID NO: 1)**.

Please delete the paragraphs on page 16, lines 13-27 and replace them with the following paragraphs:

In another aspect of the present invention, there is provided a bidentate motif capable of binding to a cytoplasmic protein comprising a tyrosine and a serine/threonine residue, said motif consisting of the following sequence alignment:

N-X-X-Y- (X) $_{1-13}$-[R/K/H/Q]-[X/Ψ] $_{2-3}$-S/T-X-P **(SEQ ID NO: 71)**

wherein X is any residue, Y is tyrosine, S/T is serine or threonine and Ψ is a ~~hydrophibic~~hydrophobic residue or an equivalent thereof.

In yet another aspect of the present invention, there is provided a bidentate motif capable of binding to a cytoplasmic protein comprising a tyrosine and a serine/threonine residue, said motif consisting of the following sequence alignment:

Y- (X) $_{1-16}$-[R/K/H/Q]-[X/Ψ] $_{2-3}$-S/T-X-P **(SEQ ID NO: 72)**

wherein X is any residue, Y is tyrosine, S/T is serine or threonine and Ψ is a ~~hydrophibic~~hydrophobic residue or an equivalent thereof.

Please delete the paragraphs on page 23, line 1 to page 25, line 20 and replace them with the following paragraphs:

In another embodiment of the present invention, it is preferred that the motif comprises a sequence selected from any one of the following sequences:

NGPYLG.....PP..HSRSLP **(SEQ ID NO: 2)**
NVHYRT.....P...KTHTMP **(SEQ ID NO: 3)**
RYFTQKEE.....TESGSGP **(SEQ ID NO: 4)
NKKYELQDRDVCE....P.RYRSVSEP **(SEQ ID NO: 5)**
NPTYSVM.....RSHSYP **(SEQ ID NO: 6)**
NIFYLIR...KSGSFPMPELKLSISFP **(SEQ ID NO: 7)**
NEEYLDLSQ.....PLEQYSPSYP **(SEQ ID NO: 8)**

NQEYLDLSM.....PLDQYSPSFP **(SEQ ID NO: 9)**
NATYKVD.....VIQRTRSKP **(SEQ ID NO: 10)**
NPEY.....HSASSGP **(SEQ ID NO: 11)**
NPDY.....WNHSLP **(SEQ ID NO: 12)**
NPSYSSNPFVNYN....KTSICSKSNP **(SEQ ID NO: 13)**
NTLY.....FNSQSSP **(SEQ ID NO: 14)**
NPVYQKTTEDEVHI...CHNQDGYSYP **(SEQ ID NO: 15)**
NPVYLKTTEEDLSIDIG..RH.SASVG **(SEQ ID NO: 16)**
NPTYKMYEGGEPDDVGGLLDADFALDPDKPTNFTNPVY **(SEQ ID NO: 17)**
NPIY.....KSAVTTVV **(SEQ ID NO: 18)**
NPLY.....KSAITTTV **(SEQ ID NO: 19)**
NPLY.....KEATSTFT **(SEQ ID NO: 20)**
NPLY.....RKPISTHT **(SEQ ID NO: 21)**
NPLY.....RGSTSTFK **(SEQ ID NO: 22)**
PGHYL.....RCDSTQP **(SEQ ID NO: 23)**
VQTYVLQ.....GDPRAVSTQP **(SEQ ID NO: 24)**
QVLYGQLL.....GSPTSP **(SEQ ID NO: 25)**
HSGYRHQVPSVQVF.....SRSESTQP **(SEQ ID NO: 26)**
WKMYEVYDA.....KS.KSVSLP **(SEQ ID NO: 27)**
KIPYFHA.....GGS.KCSTWP **(SEQ ID NO: 28)**
ELDYCLKGLKL.....P.S.RTWSPP **(SEQ ID NO: 29)**
SGDYMPM.....SPKSVSAP **(SEQ ID NO: 30)**
SFYYSEENKLPEPEELDLEPENMESVP(LDPSASSSSLP) **(SEQ ID NO: 31)**
EEIYIIM.....QSCWAFDSRKRPSFP **(SEQ ID NO: 32)**
ISQYLQN.....S.KRKSRP **(SEQ ID NO: 33)**
GTAY.....GLSRSQP **(SEQ ID NO: 34)**
***YLPQEDWAP.....TSLTRP **(SEQ ID NO: 35)**

LVAYIAFKRWNSCKQN...KQGANSRPVNQTPPPEGEKLHSDSGIS **(SEQ ID NO: 36)**

NVHY.....RTPTTHTMP **(SEQ ID NO: 37)**

NKCY.....RGRSCP **(SEQ ID NO: 38)**

NPNYTEFKFPQIKAHPWT.....KVFKSRTPP **(SEQ ID NO: 39)**

NQKYMSFTSGDKSAHGYIAAHPSST.....KTASEP **(SEQ ID NO: 40)**

NRTYYLMDPSGNAHKWCRKIQEVW.....RQRYQSHP **(SEQ ID NO: 41)**

NIFYLIRKSGSFPMPEL.....KLSISFP **(SEQ ID NO: 42)**

Preferably, these correspond to

betaR	NGPYLG.....PP..HSRSLP **(SEQ ID NO: 2)**
Acetylcholine R	NVHYRT.....P...KTHTMP **(SEQ ID NO: 3)**

Acetylcholine R alpha-5 **RYFTQKEE.....TESGSGP **(SEQ ID NO: 4)**

C-C chemokine receptor 6 NKKYELQDRDVCE....P.RYRSVSEP **(SEQ ID NO: 5)**

Middle T antigen NPTYSVM.....RSHSYP **(SEQ ID NO: 6)**

integrin alpha 1 NIFYLIR...KSGSFPMPELKLSISFP **(SEQ ID NO: 7)**

FGFR2 (KGF R) NEEYLDLSQ.....PLEQYSPSYP **(SEQ ID NO: 8)**

FGFR1 (flg) NQEYLDLSM.....PLDQYSPSFP **(SEQ ID NO: 9)**

FGFR5 NATYKVD.....VIQRTRSKP **(SEQ ID NO: 10)**

Erb4 NPEY.....HSASSGP **(SEQ ID NO: 11)**

Erb4 (second) NPDY.....WNHSLP **(SEQ ID NO: 12)**

Vaccinia virus protein A36R NPSYSSNPFVNYN....KTSICSKSNP **(SEQ ID NO: 13)**

Macrophage mannose R (MRC1) NTLY.....FNSQSSP **(SEQ ID NO: 14)**

LDLR NPVYQKTTEDEVHI...CHNQDGYSYP **(SEQ ID NO: 15)**

VLDL (rat) NPVYLKTTEEDLSIDIG..RH.SASVG **(SEQ ID NO: 16)**

LRP1 low density lipoprotein receptor-related protein 1

NPTYKMYEGGEPDDVGGLLDADFALDPDKPTNFTNPVY **(SEQ ID NO: 17)**

integrin beta 1 NPIY.....KSAVTTVV **(SEQ ID NO: 18)**

interin beta 7 NPLY.....KSAITTTV **(SEQ ID NO: 19)**

integrin beta 3 NPLY.....KEATSTFT **(SEQ ID NO: 20)**

integrin beta 5 NPLY.....RKPISTHT **(SEQ ID NO: 21)**

integrin beta 6 NPLY.....RGSTSTFK **(SEQ ID NO: 22)**

G-CSFR1 (second) PGHYL.....RCDSTQP **(SEQ ID NO: 23)**

G-CSFR1 VQTYVLQ.....GDPRAVSTQP **(SEQ ID NO: 24)**

g-csf-r QVLYGQLL.....GSPTSP **(SEQ ID NO: 25)**

IL-6B (gp130) HSGYRHQVPSVQVF.....SRSESTQP **(SEQ ID NO: 26)**

leptinR. WKMYEVYDA.....KS.KSVSLP **(SEQ ID NO: 27)**

prolactinR... KIPYFHA.....GGS.KCSTWP **(SEQ ID NO: 28)**

insulinR ELDYCLKGLKL.....P.S.RTWSPP **(SEQ ID NO: 29)**

irs-1 .... SGDYMPM.....SPKSVSAP **(SEQ ID NO: 30)**

IGFI R SFYYSEENKLPEPEELDLEPENMESVP(LDPSASSSSLP) **(SEQ ID NO: 31)**

flt3 R EEIYIIM.....QSCWAFDSRKRPSFP **(SEQ ID NO: 32)**

VEGFR2 (FLK1) ISQYLQN.....S.KRKSRP **(SEQ ID NO: 33)**

PDGF R-alpha GTAY.....GLSRSQP **(SEQ ID NO: 34)**

IL-9R ***YLPQEDWAP.....TSLTRP **(SEQ ID NO: 35)**

p75 NTR

LVAYIAFKRWNSCKQN...KQGANGRPVNQTPPPEGEKLHSDSGIS(phosphorylated) **(SEQ ID NO: 36)**

(SEQ ID NOS 43-60 are disclosed respectively in order of appearance)

GM-CSF receptor βc subunit	:NGPYLGPP.....HSRSL
erbB4	:NPDY.....WNHSL
fibroblast growth factor receptor 1 (flg)	:NQEYLDLSIPLD.....QYSPSF
fibroblast growth factor receptor 2 (KGF	:NEEYLDLSQPLE.....QYSPSY
fibroblast growth factor receptor 5	:NATYKVDVI.....QRTRSK
low-density lipoprotein receptor-related	:NPTYKMYEGGEPDDVGGLLDADFALDPD....KPTNFTN
low density lipoprotein receptor	:NPVYQKTTEDEVHICHN.....QDGYSY
very low density lipoprotein receptor	:NPVYLKTTEEDLSIDIG.....RHSASV
Neuronal acetylcholine receptor protein,	:NVHY.....RTPTTHTM
protein tyrosine phosphatase receptor N	:NKCY.....RGRSC
glycogen synthase kinase 3 alpha	:NPNYTEFKFPQIKAHPWT.....KVFKSRTP
p21-activated kinase 3	:NQKYMSFTSGDKSAHGYIAAHPSST.....KTASE
3-phosphoinositide dependent protein	:NRTYYLMDPSGNAHKWCRKIQEVW.....RQRYQSH
integrin alpha 1 (laminin/collagen receptor)	:NIFYLIRKSGSFPMPEL.....KLSISF
integrin beta 1 (integrin VLA-4 beta)	:NPIY.....KSAVTTV
integrin beta 3(platelet glycoprotein IIIa)	:NPLYKEA.....TSTFTN
integrin beta-6	:NPLYR.....GSTSTF
integrin beta-7	:NPLYKS.....AITTTI

MOTIF (forward) **n-X-X-Y-X(3,17)-[RKHQ]-X(2,3)-[ST]-X-P**

EGFR RYSSDPTGALTEDSIDDTFLPVPEYINQSVPKRPAGSVQNPVY.. (NPEY) **(SEQ ID NO: 61)**

Erb2 KTLSPGKNGVVKDVFTF.....GGAVENPEY **(SEQ ID NO: 62)**

Voltage-depend T-type Ca chan. alpha-1G subunit RTHSLP.....NDSY **(SEQ ID NO: 63)**

EPO R SDGPYSNPYENSLIPAAEPLPPSYVACS **(SEQ ID NO: 64)** (Y NB in PI 3-K; S is end of protein, JBC 270: 23402)

MOTIF (reverse) **[RKHQ]-X(2,3)-[ST]-X-P-X(0,33)-N-X-X-Y**

TRHR receptor HFSTELD **(SEQ ID NO: 65)**

IL-2R beta NQGYFFFHLPDALEIEACQVYFTYDPYSEEDPDEGVAGAPTGSSP **(SEQ ID NO: 66)**

Please delete the paragraph on page 42, lines 2-10 and replace it with the following paragraph:

Pulldown experiments were performed as previously described (Stomski et al., 1999). Peptides were synthesized with a biotin-N-Hydroxysuccinimide (biotin-NHS) N-terminus and were HPLC purified (Mimotopes, Victoria). Peptide sequences were biotin-NHS-KGGFDFNGPYLGPPHSRSLPDGG **(SEQ ID NO: 67)** (non-phospho-Tyr577/non-phospho-Ser585), biotin-NHS-KGGFDFNGP(pY)LGPPHSRSLPDGG **(SEQ ID NO: 68)** (phospho-Tyr577/non-phospho-Ser585), biotin-NHS-KGGFDFNGPYLGPPHSR(pS)LPDGG **(SEQ ID NO: 69)** (non-phospho-Tyr577/phospho-Ser585) and biotin-NHS-KGGFDFNGP(pY)LGPPHSR(pS)LPDGG **(SEQ ID NO: 70)** (phospho-Tyr577/phospho-Ser585).

Please delete the paragraph on page 51, line 26 to page 52, line 27 and replace it with the following paragraph:

The identification of a novel phosphotyrosine/phosphoserine bidentate motif that is important in regulating cell survival in these studies prompted us to examine whether other cell surface receptors may also contain similar motifs. Phosphorylated Tyr577 of βc binds Shc via its PTB domain whereas phosphorylated Ser585 binds 14-3-3. We therefore scanned the cytoplasmic domains of cell surface receptors for a PTB binding site followed by a 14-3-3 binding site using software available to the skilled addressee. The PTB domain of Shc recognizes a N-X-X-Y motif (where Y is phosphorylated). 14-3-3 was originally demonstrated to binding two possible motifs; a mode 1 site (R-S-X-S/T-X-P) or a mode 2 site (R-X/Ψ-X/Ψ-X/Ψ-S/T-X-P)(where S or T is phosphorylated and Ψ is a hydrophobic

residue). Variations on these prototypic 14-3-3 binding motifs have since been reported with K, H or Q also being tolerated at the -3 and -4 positions relative to the phosphoserine/phosphothreonine. In addition, the proline at the +2 position, which has been reported to be important for the correct exit of the bound protein from the binding groove of 14-3-3, has been found to be dispensible if the 14-3-3 binding motif occurs close to the C-terminus of a protein. Searching for motifs that allow these variations, we have identified conserved putative bidentate tyrosine/serine motifs in a range of cell surface receptors (Table 1). In addition to the noteable prevalence of such a bidentate motif in cell surface receptors, it is also striking that in some cases this motif appears to be conserved within specific members of receptor families such as the FGF, LDL and integin receptor families. Alignment of these motifs suggests a putative consensus bidentate motif, N-X-X-Y-$(X)_{1-13}$-[R/K/H/Q]-[X/Ψ_{2-3}-S/T-X-P **(SEQ ID NO: 74)** (where X is any residue, Y is phosphotyrosine, S/T is phosphoserine or phosphothreonine and Ψ is a hydrophobic residue). We also considered the possibility that receptors may also utilize alternative motifs in which the tyrosine residue was not part of a PTB binding site but rather an SH2 binding site. Searching for an adjacent tyrosine residue/14-3-3 binding site, we identified alternative putative bidentate motifs in a range of cell surface receptors. Alignment of these motifs gave the consensus Y-$(X)_{1-16}$-[R/K/H/Q]-[X/Ψ_{2-3}-S/T-X-P **(SEQ ID NO: 72)**. Our finding that the Tyr577/Ser585 bidentate motif is important in regulating cell survival in response to GM-CSF and that similar motifs are also found in other cell surface receptors suggests that this novel motif may play a fundamental role in regulating intracellular signalling in response to a wide range of cytokines and growth factors.

Please delete Table 1 on page 52, line 29 to page 54, line 9 and replace it with the following paragraph:

Table 1

PILE UP:

betaR .... ::GPYLG.....PP..HSRSLP **(SEQ ID NO: 2)**

Acetylcholine R (ISOFROM?) NVHYRT..........P...KTHTMP **(SEQ ID NO: 3)**
Acetylcholine R alpha-5 **RYFTQKEE.........TESGSGP **(SEQ ID NO: 4)**
(CONSERV?)
C-C chemokine receptor 6 NKKYELQDRDVCE....P.RYRSVSEP **(SEQ ID NO: 5)**
Middle T antigen NPTYSVM.............RSHSYP **(SEQ ID NO: 6)**
integrin alpha 1 NIFYLIR...KSGSFPMPELKLSISFP **(SEQ ID NO: 7)**
FGFR2 (KGF R) NEEYLDLSQ........PLEQYSPSYP **(SEQ ID NO: 8)**
FGFR1 (flg) NQEYLDLSM........PLDQYSPSFP **(SEQ ID NO: 9)**
FGFR5 NATYKVD...........VIQRTRSKP **(SEQ ID NO: 10)**
Erb4 NPEY.................HSASSGP **(SEQ ID NO: 11)**
Erb4 (second) NPDY.................WNHSLP **(SEQ ID NO: 12)**
Vaccinia virus protein A36R NPSYSSNPEVNYN....KTSICSKSNP **(SEQ ID NO: 13)**
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LDLR NPVYQKTTEDEVHI...CHNQDGYSYP **(SEQ ID NO: 15)**
VLDL (rat) NPVYLKTTEEDLSIDIG..RH.SASVG **(SEQ ID NO: 16)** (near
end of protein)
LRP1 low density lipoprotein receptor-related protein 1
NPTYKMYEGGEPDDVGGLLDADFALDPDKPTNFTNPVY **(SEQ ID NO: 17)**

integrin beta 1 NPIY..............KSAVTTVV **(SEQ ID NO: 18)**
(end of protein)
integrin beta 7 NPLY..............KSAITTTV **(SEQ ID NO: 19)**
(end of protein)
integrin beta 3 NPLY..............KEATSTFT **(SEQ ID NO: 20)**
(end of protein)
integrin beta 5 NPLY..............RKPISTHT **(SEQ ID NO: 21)**
(end of protein)
integrin beta 6 NPLY..............RGSTSTFK **(SEQ ID NO: 22)**

G-CSFR1 (second) PGHYL.............RCDSTQP **(SEQ ID NO: 23)**

G-CSFR1 VQTYVLQ.........GDPRAVSTQP **(SEQ ID NO: 24)**

g-csf-r (CHECK?) QVLYGQLL.............GSPTSP **(SEQ ID NO: 25)**
IL-6B (gp130) HSGYRHQVPSVQVF.....SRSESTQP **(SEQ ID NO: 26)**

leptinR. WKMYEVYDA.........KS.KSVSLP **(SEQ ID NO: 27)**

prolactinR... KIPYFHA.........GGS.KCSTWP **(SEQ ID NO: 28)**

insulinR ELDYCLKGLKL......P.S.RTWSPP **(SEQ ID NO: 29)**

irs-1 .... SGDYMPM............SPKSVSAP **(SEQ ID NO: 30)**

IGFI R
SFYYSEENKLPEPEELDLEPENMESVP(LDPSASSSSLP)[illegible]=survl.**(SEQ ID NO: 31)**

flt3 R EEIYIIM.....QSCWAFDSRKRPSFP **(SEQ ID NO: 32)**

VEGFR2 (FLK1) ISQYLQN............S.KRKSRP **(SEQ ID NO: 33)**

PDGF R-alpha GTAY..............GLSRSQP **(SEQ ID NO: 34)**

IL-9R ***YLPQEDWAP.....TSLIRP (CONSERV?) **(SEQ ID NO: 35)**

p75 NTR
LVAYIAFKRWNSCKQN...KQGANSRPVNQTPPPEGEKLH**S**DSGIS(phosphorylated)
(SEQ ID NO: 36)

MOTIF (forward) n-X-X-Y-X(3,17)-[RKHQ]-X(2,3)-[ST]-X-P

EGFR RYSSDPTGALTEDSIDDTFLPVPEYINQSVPKRPAGSVQNPVY.. (NPEY)
(SEQ ID NO: 61)

Erb2 KTLSPGKNGVVKDVFTF.....GGAVENPEY
(SEQ ID NO: 62)

Voltage-depend RTHSLP.....NDSY
(SEQ ID NO: 63)

T-type Ca chan.
alpha-1G subunit

EPO R SDGPYSNPYENSLIPAAEPLPPSYVACS **(SEQ ID NO: 64)**
(Y NB in PI 3-K; S is end of protein, JBC 270: 23402)

MOTIF (reverse) [RKHQ]-X(2,3)-[ST]-X-P-X(0,33)-N-X-X-Y

TRHR receptor HFSTELD **(SEQ ID NO: 65)**

IL-2R beta NQGYFFFHLPDALEIEACQVYFTYDPYSEEDPDEGVAGAPTGSSP **(SEQ ID NO: 66)**

AMENDMENTS TO THE ABSTRACT

Please substitute the following paragraph(s) for the abstract now appearing in the currently filed specification: